I. INTRODUCTION

A. Overview of the Manuals of Operations

The purpose of the Manuals of Operations is to provide documentation necessary for orientation, training, implementation, and evaluation with regard to the study entitled "Interventions for Risk Factors in Pregnant Women in Washington D.C.: An Integrated Approach," also known as Project HOPE. These documents will be used primarily by personnel and program staff as a reference on the routine implementation of the protocol.

Three Manuals of Operations have been developed for Project HOPE. These manuals detail the specific steps that must be taken to (1) identify and recruit potential eligible subjects, (2) conduct the intervention, and (3) conduct the evaluation. Further, they describe the protocol objectives and the operational requirements needed to achieve these objectives. Revisions and additions to the Manuals will be distributed to study personnel as dated replacement pages to be inserted in the existing Manuals. These revisions/additions will ensure that all protocol requirements are documented and implemented. In addition, the Manuals of Operations will serve as a historical summary of the operations of this project.

B. NIH-DC Initiative: Background and Study Rationale

In 1990, the infant mortality rate in the District of Columbia was 20 per 1000 live births, a rate higher than that of any of the 50 states and among the highest for any city with a population greater than 500,000. The infant mortality rate is expressed in terms of the number of infants who die in their first year of life per 1,000 live births. The infant mortality rate decreased from 29 per 1000 in 1970 to a low level of 18 per 1000 in 1983. The rate increased to 23 per 1000 in 1989. A major determinant of the high infant mortality in the District of Columbia is the high rate of low weight births. During this period the low birth weight (LBW) rate among African Americans increased from 13% to 17.6%.

In response to the need to reduce infant mortality in the District of Columbia and to eliminate the disparity in minority populations, the National Institute of Child Health and Human Development (NICHD), in conjunction with the National Institutes of Health Office of Research on Minority Health and the National Institute for Nursing Research, began a collaborative effort to develop coordinated projects designed to better understand the reasons for the high rate of infant mortality in the District of Columbia, and to develop and evaluate intervention projects aimed at reducing the number of infants in the District who are at increased risk of dying in their first year of life. The project, entitled "*The NIH-DC Initiative to Reduce Infant Mortality among Minority Populations in Washington, DC*" (NIH-DCI) began in the fall of 1992 and was funded for five years.

The grantees in the first phase of the NIH-DCI included Children's National Medical Center, the DC Commission of Public Health, DC General Hospital, Georgetown University, Howard University, and the University of the District of Columbia. The Greater Southeast and Providence Hospitals (affiliated with Georgetown University), the George Washington University (affiliated with Children's Hospital), the DC Office on Latino Affairs, and the Department of Corrections (in partnership with the DC Commission of Public Health) were also in the program. RTI was selected as the Data Coordinating Center for the program in 1993.

The goal of Phase I was to better understand the reasons why some women may be at higher risk of having a LBW infant and why some infants are at increased risk of dying early in life. Populations studied included the following: inner-city pregnant or postpartum women and/or their children recruited through primary care facilities, public health clinics or inpatient settings; students in 7th grade in Washington DC middle schools; and infants up to age 36 months who were treated in hospital emergency rooms or admitted to hospitals with injuries. The following eight studies were approved and carried out during the period:

- Pride in Parenting: Parenting Education Impacts on Health Care Utilization
- The Association of Neonatal Outcomes with the Characteristics of Neonatal Units
- Lack of Age-Appropriate Immunizations Among Infants and Young Children Born in the District of Columbia
- Preventing Adolescent Pregnancy
- The Prevention of Fetal Alcohol Effects in the District of Columbia
- Barriers, Motivators, and Facilitators of Prenatal Care Utilization in Washington D.C.: A Program of Research
- The Prevention of Childhood Injuries
- Evaluation of Health Systems for Pregnant Medicaid Recipients in the District of Columbia.

The second 5-year phase of the program was funded starting on May 1, 1998 with four grantees: The Children's National Medical Center, Georgetown University, George Washington University, and Howard University. RTI was also selected as the Data Coordinating Center for this phase. In this phase, the results of the Phase I studies are being combined with other information to develop and test strategies to lower risks for adverse pregnancy outcomes. Two studies--Adolescent Pregnancy Prevention Phase II and Project HOPE--were approved by the Scientific Advisory Committee appointed by NICHD.

C. Interventions for Risk Factors: Protocol Overview

Project HOPE is designed to develop, implement and evaluate an integrated clinic-based intervention targeting psychosocial risk (specifically, depression and partner abuse) and cigarette smoking among pregnant women. Study procedures will identify and provide intervention for one or both risk factors, depending on the individual woman's needs. Baseline screening and subsequent assessments will enable the Interventionist/Pregnancy Advisor (PA) to offer an education/counseling package that is customized to the changing needs of each woman. These intensive interventions will continue with the women up to 6-8 weeks postpartum. Periodic evaluations will be administered during pregnancy and 6-10 weeks postpartum to assess the efficacy of the intervention. Women receiving usual care in the same prenatal clinics will serve as the comparison group.

1. Primary Objective

The goal of Project HOPE is to reduce the prevalence and severity of two specific risk factors linked to adverse pregnancy outcomes by providing health behavior counseling to pregnant women of African American and Latina race/ethnicity in Washington, D.C. A secondary goal of the integrated intervention program is to improve pregnancy outcomes as measured by infant birth weight and gestational age.

Statistics for 1998 indicate that 13.1% of District infants of all races were born at LBW, exceeding the national figure of 7.6% LBW infants. Nationwide, 28% of the excess infant mortality for African Americans compared to whites is attributable to LBW. In the District of Columbia, both preterm birth (PTB) and LBW are nearly three times more common among African American women as compared to white women. Any attempt to reduce infant mortality in the predominantly African American population of the District must address PTB and LBW, and risk factors for their occurrence.

Psychosocial risk and smoking were selected for intervention in the study, with consideration given to the fact that both are linked to adverse pregnancy outcomes, are relatively common in the population, and are amenable to change. For the purposes of this study, psychosocial risk is defined as depression and/or partner abuse, which are linked to adverse pregnancy outcomes of LBW and PTB. Depression and other psychosocial risks have also been associated with negative health behaviors (such as the use of tobacco, alcohol, or drugs) and with a failure to make and keep medical appointments, factors that may further contribute to poor pregnancy outcomes. Approximately 25% of women in the target population are estimated to experience depression and/or partner abuse. Previous research indicates that effective interventions can be delivered in conjunction with prenatal care.

Cigarette smoking is a major risk factor for adverse pregnancy outcomes; smoking directly impacts fetal growth and has a documented association with PTB. Estimates suggest that approximately 31% of this population is at risk for adverse pregnancy outcomes due to smoking behavior. Fortunately, there is evidence that women who significantly reduce their smoking or quit smoking early in pregnancy may deliver infants with improved birth weights.

While psychosocial risks and smoking often coexist in pregnant woman, most studies have targeted single risk factors. This may explain the modest effectiveness of many prenatal intervention studies. An innovative aspect of this project is its attempt to identify and provide an integrated intervention for those psychosocial and behavioral risk factors that have shown significant association with poor pregnancy and postpartum outcomes. Evaluations are proposed which assess the effectiveness of the intervention with regard to reducing the risk factors as well as to improving maternal and infant outcomes.

2. Specific Aims

There are two broad categories of hypotheses for this study:

1. Improvement in targeted risk factors.
2. Improvement in pregnancy outcomes.

The evaluation component of this study will assess the overall impact of the integrated intervention on the population, the impact of the two risk-specific components of the intervention on birth outcomes, and the prevalence of the targeted risk factors among the study population at predetermined time points during pregnancy and postpartum.

3. Variables of Interest and Their Measurement

Two sets of outcome measures will be collected. The first will be an assessment battery consisting of self-report measures and a biological measure of salivary cotinine level. This battery will assess the efficacy of the intervention by measuring changes in the risk factors at the individual and group (intervention versus usual care) levels. These outcome measures will be collected at baseline, in each subsequent trimester of pregnancy, and after delivery of the index pregnancy (approximately 6-10 weeks postpartum).

Data abstraction from clinic and hospital medical records comprises the second type of outcome evaluation. It will be implemented to examine the overall success of the intervention as measured by pregnancy outcomes.

4. Study Design

Pregnant women of African American or Latina race/ethnicity who are DC residents and at least 18 years of age will be eligible for this project. They will be recruited at participating prenatal care clinics through 28 weeks gestational age in their pregnancies.

Women meeting all eligibility criteria and consenting to participate will be screened for psychosocial risk (depression, partner abuse) and smoking (including exposure to environmental tobacco smoke). The baseline evaluation questionnaire will be administered prior to the participant's next prenatal care visit when intervention activities are scheduled to start. All reasonable attempts will be made to contact, schedule, and interview enrolled women prior to the cutoff date. A system of stratified randomization (taking into account the number and type of declared risks) will be used to assign women who complete the baseline interview in equal proportions to either the intervention or usual care group.

Women assigned to the intervention group will meet with a trained PA at each prenatal visit and at two postpartum sessions in order to receive individualized counseling targeting their area(s) of declared risk. They will be evaluated periodically by the PAs for all risk factors not previously declared and, if additional risks are identified, will receive intervention for these as well. Women assigned to the usual care group will meet with their primary care providers as per standard clinic practice.

Components of the integrated intervention targeting depression will be based on the Cognitive-Behavioral theoretical model, and intervention content for partner abuse will focus on developing a safety plan. The Stages of Change model will provide the framework for the smoking cessation intervention. A brief educational component focusing on healthy reproductive practices will also be provided to all women in the intervention group.

The prenatal intervention is designed to be integrated into the woman's prenatal care visit plan. Women who enter the study at the end of the eligibility period (28 weeks gestation) and deliver their infants at term will have a minimum exposure of four prenatal and two postnatal intervention sessions. Women entering earlier in pregnancy will have an opportunity for greater exposure to the intervention. The PA will follow a delineated sequence of sessions but will be prepared to adjust each session to address any urgent issue that presents.

5. Sample Size and Participating Hospitals

Over a two-year period, 4,000 women will be screened in the study. It is estimated that as many as 1,750 of these women will have one or more declared risk factors.

Recruitment for Project HOPE is scheduled to begin in June 2001 with up to five hospitals. This will be followed by a phase-in period for up to three additional sites.

Recruitment sites include Washington Hospital Center, Columbia Hospital for Women Medical Center, George Washington University Medical Center, Howard University Hospital, and Chartered Health.

D. The Evaluation Component

The evaluation component of Project HOPE consists of:

- telephone interviews conducted with all women recruited into Project HOPE;
- saliva specimens collected from all women to test for cotinine to provide a biological marker for exposure to cigarette smoke; and
- medical record abstractions to obtain information regarding pregnancy outcomes and medical conditions known to increase the risk of adverse pregnancy outcomes.

The focus of this Manual of Operations is on procedures for conducting the evaluation telephone interviews. A woman may be interviewed as many as four times and as few as three times, depending on when in her pregnancy she is recruited into the study. This is because the study is designed to obtain evaluation interviews from women once per trimester and once postpartum, with approximately four weeks between interviews. Therefore, all women will receive the baseline interview immediately after time of recruitment, one or two prenatal follow-up interviews between recruitment and delivery (depending on her gestational age at time of recruitment), and one postpartum follow-up interview after delivery.

E. Study Organization

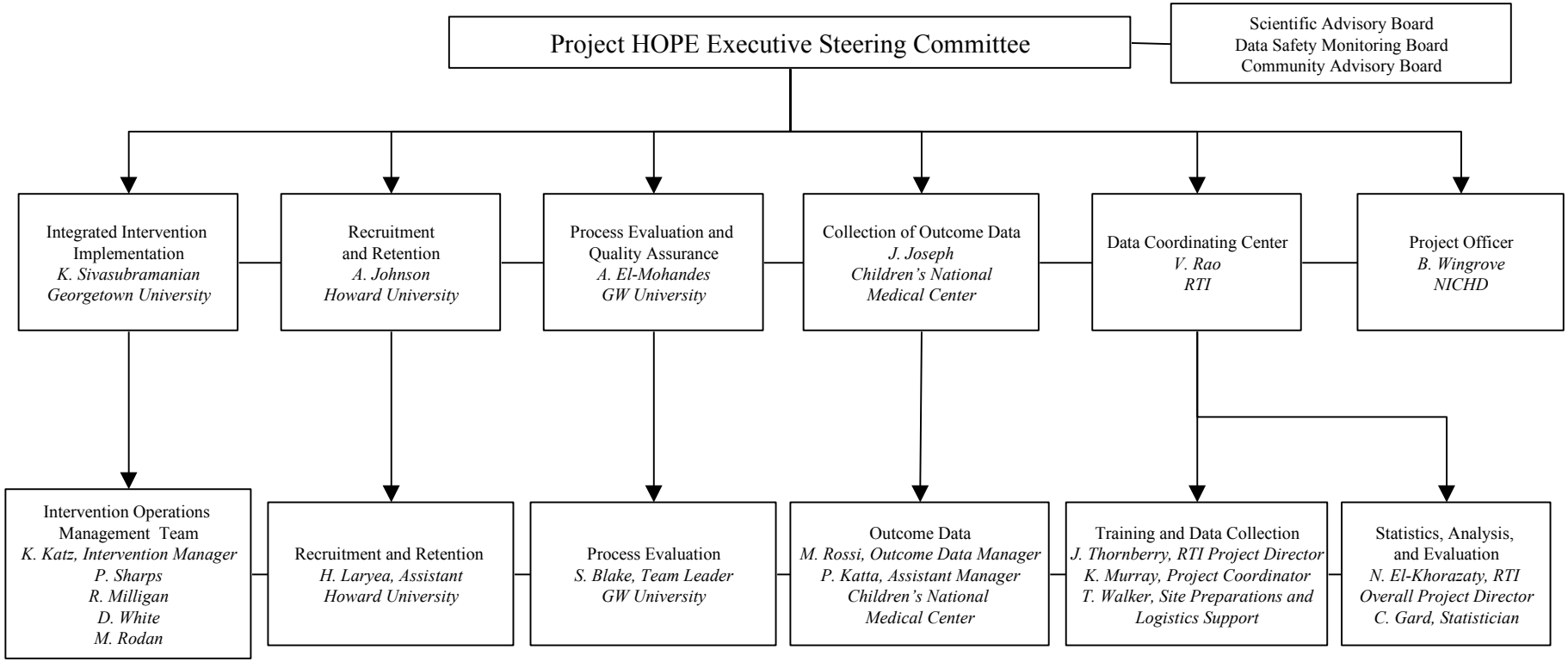
1. Administration

The major organizational components of Project HOPE include the NIH-DC Initiative Cooperative Agreement Grantee Organizations: Children's National Medical Center (PI: Jill G. Joseph, M.D., Ph.D.), Georgetown University Medical Center (PI: K.N. Siva Subramanian, M.D.), George Washington University Medical Center (PI: Ayman A.E. El-Mohandes, M.D., M.P.H.), Howard University (PI: Allan A. Johnson, Ph.D., L.N.); a Data Coordinating Center (The Research Triangle Institute, PI: A. Vijaya Rao, Ph.D.); and the NICHD Program Office (Program Officer, Barbara K. Wingrove, M.P.H.).

The protocol was developed by the investigators from the four Primary Grantee sites, the Data Coordinating Center (DCC), and NICHD. They continue to have central responsibility for the conduct of the study. The Project HOPE Executive Steering Committee, comprised of the four PIs of the Primary Grantee sites, the DCC, and the NICHD representative, provides the scientific direction for the study (see Exhibit I-1). Each of the four PIs is responsible for one of the following main areas: (1) Integrated intervention implementation, (2) Recruitment and retention, (3) Process evaluation and quality assurance, and (4) Collection of outcome data. Subgroups of the Executive Steering Committee and their designees provide guidance on day-to-day issues arising from the implementation of the study, such as conduct of the intervention, data collection, quality control, analysis, and evaluation.

In addition, the Primary Grantee site PIs provide the link between the prenatal care sites at which women will be recruited and the study management. Finally, study activities are carried out by staff recruited through, and supervised by, the Primary Grantee sites or the DCC.

Exhibit I-1. Healthy Outcomes of Pregnancy Education (Project HOPE) Organizational Chart



There will be an intervention team at each of the clinical sites. This team will consist of PAs and Pregnancy Advisor Assistants (PAAs). The actual number of PAs at each site will depend on the number of enrollees. Conduct of the intervention is guided by an Intervention Technical Assistance Team consisting of experts in each component of the intervention and carried out by an Intervention Operations Management Team (see Exhibits I-2 and I-3). Overall responsibility for activities of the Intervention Operations Management Team rests with the Intervention Manager who reports directly to the Project HOPE Executive Steering Committee and serves as an ex-officio member of that group. In order to facilitate conduct of the intervention, the Intervention Manager and the PAs are employed by a single institution represented on the Steering Committee. In this way staff supervision and authority to maintain the quality of the intervention is aligned with responsibility for its implementation.

Exhibit I-2. Intervention Technical Assistance Team

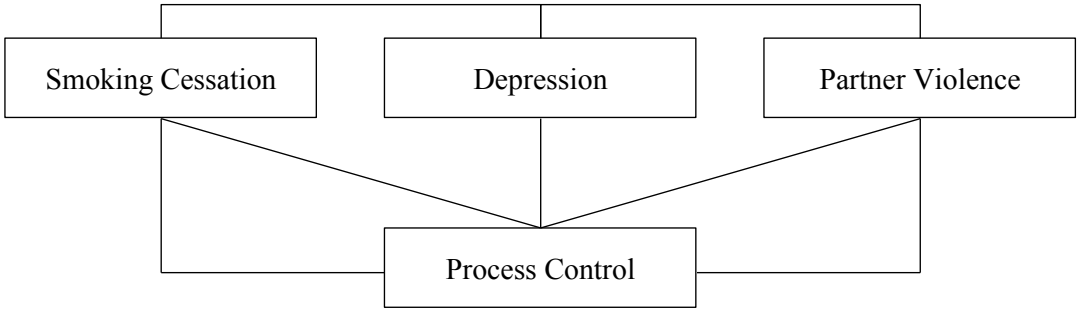
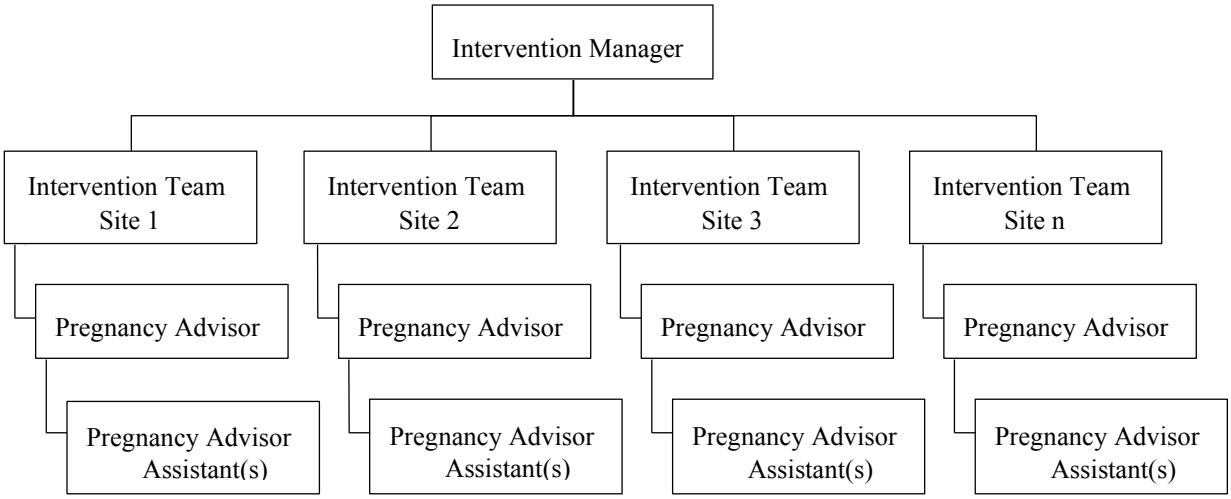


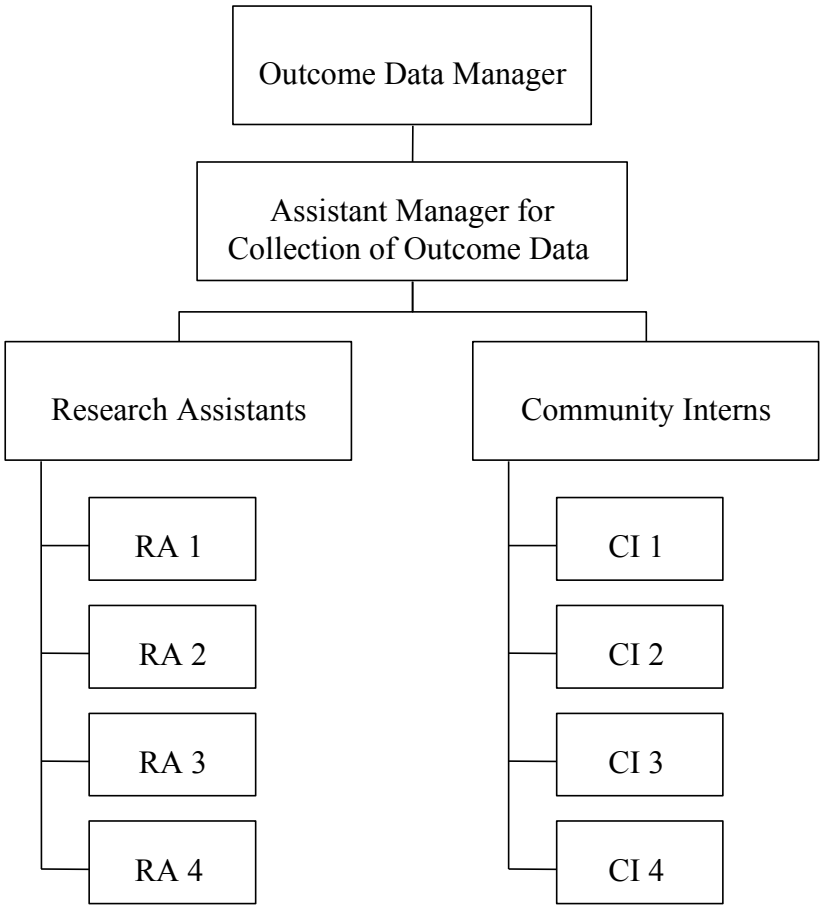
Exhibit I-3. Intervention Operations Management Team



The Collection of Outcome Data Team consists of an Outcome Data Manager, an Assistant Manager for Collection of Outcome Data, Research Assistants (RAs), and Community Interns (CIs) (Exhibit I-4). This team is responsible for the collection of all outcome data required for the conduct of the study evaluation. The RAs will work at a single location to schedule and administer the telephone evaluations. The Assistant Manager and the Community Interns under his/her supervision are specifically responsible for medical records abstractions. The Outcome Data Manager has overall responsibility for the activities of the Collection of Outcome Data Team and reports to the Project HOPE Executive Steering Committee as well as serves as an ex-officio member.

The DCC provides the study materials, trains the RAs, CIs and the intervention teams in all aspects of data acquisition (intervention and outcome data related), and provides technical guidance on data collection. The DCC is responsible for design implementation and monitoring of methods for data recording and transfer (with special attention to data quality and completeness). The data center staff will collaborate with the Intervention Team and the Outcome Data Team in numerous ways throughout the conduct of the study. The DCC will prepare analytical reports from the study data to be presented to the Project HOPE Executive Steering Committee at regular intervals. The DCC will also prepare interim reports to be presented to the DSMB (Data Safety Monitoring Board).

Exhibit I-4. Collection of Outcome Data



2. Study Monitoring

The conduct and progress of the study will be monitored internally and externally. The internal monitoring will be carried out by both identified individuals and subcommittees of the Steering Committee. The external monitoring, i.e. oversight, will be the responsibility of the Data Safety Monitoring Board (DSMB) appointed by the NICHD.

The intervention activities and delivery will be monitored by the Intervention Oversight team. The DCC will provide support to these monitoring activities with reports based on the data from the intervention tracking system and the process evaluation data. These reports will include planned and ad hoc reports as needed. The DCC staff will work with the Intervention Oversight team in designing the format and conduct of these routine reports.

Conduct of the evaluation will be monitored jointly by the Outcome Data Manager and the DCC Co-PI with responsibility in this area. This person, and other data collection experts at the DCC, will work with the Outcome Data Manager in designing systems for monitoring the evaluation data acquisition activities and implementing the systems of feedback and reporting. In large measure, this monitoring will utilize computer generated periodic reports from the DCC based on review of the accumulated data.

The key study activities--recruitment and retention, intervention, data collection and data quality, data analysis, and reporting of study data--will be monitored by committees chaired by a Primary Grantee site PI. The membership of these committees will include an investigator from the DCC, representatives of study investigators, and the NICHD program office. The DCC will organize and present reports for review by the monitoring committees.

The progress and performance of the study will be reviewed by the entire Steering Committee every quarter.

The DSMB will be established to review and interpret study data in order to ensure the safety of study subjects and provide NICHD with information on the progress the study. The members of the DSMB will be chosen by the NICHD and will be experts in fields that are relevant to study. The Chairperson will be appointed by the NICHD. An NICHD staff person will serve as executive secretary of the DSMB and liaison to the Steering Committee.

Plans for the activities of the DSMB can be determined only after the board is constituted. Generally DSMBs expect regularly scheduled reports on the status and progress of components of the study. They also often expect to periodically examine the effectiveness of the intervention by examining statistical comparisons of the usual care and intervention groups-either blinded regarding assignment or labeled. The statistical techniques of sequential monitoring and choice of blinded or labeled comparisons will be determined after consultation with DSMB.